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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/600,521	08/27/2001	Jian-Yun Dong	22488-710	7109

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EXAMINER
AKHAVAN, RAMIN

ART UNIT	PAPER NUMBER
1636	12

DATE MAILED: 09/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE

Office Action Summary	Application No. 09/600,521	Applicant(s) DONG ET AL.	
	Examiner Ramin (Ray) Akhavan	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 47-112 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 47-112 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☑ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121 and 372. This application contains the following inventions or group of inventions that are not so linked as to form a single inventive concept under PCT Rule 13.1. In accordance with 37 CFR 1.499, in response to this action applicant is required to elect a single invention to which the claims must be restricted. The groups are as follows:

I. Claims 47-51, 54 and 57 drawn to a method for inducing cell death using an inducible promoter in a construct introduced into a mixture of cells that do and do not express apoptosis-mediating receptor where the apoptosis-signaling ligand is an antibody.

II. Claims 47-50, 52, 54, 57, 60-67 and 74-85 drawn to a method for inducing cell death in a mixture of cells that do and do not express apoptosis-mediating receptor where the ligand responsible for inducing cell death is expressed using a vector, where expression is under control of an inducible promoter.

III. Claims 47-51 and 56 drawn to said method in claim 47 where the ligand inducing cell death is an antibody introduced into a group of cells expressing Fas (FasL receptor).

IV. Claims 47-50, 52, 56, 60-67 and 74-85 drawn to said method in claim 47 where the ligand inducing cell death is expressed using a vector introduced into cells already expressing Fas, where the vector contains an inducible promoter.

V. Claims 47-51 and 55 drawn to said method in claim 47 where the ligand inducing cell death is an antibody introduced into a group of cells that do not express Fas.

VI. Claims 47-50, 52, 55, 60-67 and 74-85 drawn to said method in claim 47 where the ligand inducing cell death is expressed used a vector introduced into a group of cells that do not express Fas.

VII. Claims 47, 54, 57, 60-67 and 85 drawn to a method of inducing cell death where the ligand inducing death is selected from a group consisting of Bax, Bad, Bak and Bik and the ligand is expressed using a vector introduced into a mixture of cells that do and do not express the receptor Fas.

VIII. Claims 47, 56, 60-67 and 85 are drawn to a method of inducing cell death where the ligand inducing cell death is selected from a group consisting of Bax, Bad, Bak and Bik and the ligand is expressed using a vector introduced into a group of cells that do express the receptor Fas.

IX. Claims 47, 56, 60-67 and 85 are drawn to a method of inducing cell death where the ligand inducing cell death is selected from a group consisting of Bax, Bad, Bak and Bik and the ligand is expressed using a vector introduced into a group of cells that do not express the receptor Fas.

X. Claims 47, 58-73 are drawn to a method of inducing cell death where an expression vector encoding the effector ligand is introduced into a group of cells that are contained in a solid tumor.

XI. Claims 86-96 and drawn to an adenoviral expression vector encoding a ligand or FasL wherein said vector comprises a tissue-specific inducible conditional promoter.

XII. Claims 97-104 and 111 drawn to an adenoviral expression vector comprising a tetracycline-responsive element, also encoding a transactivator for the response element and encoding a protein regulated by the response element, wherein said protein can be FasL.

XIII. Claims 105-107 and 112 are drawn to an adenoviral expression vector comprising characteristics of claim 97 but further comprising a gene encoding a reporter protein encoded as a fusion protein, wherein the reporter protein is green fluorescent protein.

XIV. Claims 108-110 are drawn to an adenoviral expression vector comprising an encoded fusion protein that causes tissue-specific localization of the target protein.

The inventions listed in Groups I-XV do not relate to a single general inventive concept under PCT Rule 13.1, because there is no unity of invention under PCR Rule 13.2 which states that unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features (i.e. technical features that define a contribution which each of the inventions considered as a whole makes over the prior art). The inventions listed above lack the same or corresponding technical features for the following reasons:

The invention in group I is drawn to a special technical feature involving expression of the apoptosis-signaling ligand (e.g. FasL) as regulated by a conditional (i.e. inducible) promoter in a vector that is introduced into cells or mixture of cells expressing or not expressing the receptor for the ligand, where the ligand is an antibody. This feature is different from the special technical feature in Group II, where an inducible promoter in an expression system is used to express FasL protein. Notably, *Larregina et al.* describe just such a special technical feature. *Larregina et al. Fas L induces Fas/Apo1-mediated apoptosis in human embryonic kidney 293 cells routinely used to generate E1-deleted adenoviral vectors. Gene Therapy; 5: 563-568 (April. 1998) Larregina et al.*, see Abstract (remarking that to obviate an obstacle of massive cell death after transfection, adenoviral vectors expressing FasL protein under the control of tissue-specific and/or inducible promoter elements were generated). Group III defines the special technical feature that the cells into which the antibody of Group I is introduced are of a population of cells expressing Fas. Similarly the special technical feature of Group IV is that the inducible vector system is introduced into a population of cells all expressing Fas. Again, *Larregina et al.* teach an inducible vector system in a population of cells expressing Fas. *Id.*

Groups V and VI are drawn to a special technical feature not contained in each other nor in the preceding Groups. First, in Group V the ligand inducing cell death is an antibody and the cell population acted upon is a group of cells that do not express the cognate death receptor – Fas. Group VI shares the feature with Group V that the ligand acts on a group of cells that do not express Fas (unlike the preceding groups) but differs from Group V in that the ligand FasL protein expressed using an expression system, versus an antibody-based system.

Groups VII-IX do not share the special technical feature with the preceding groups in that the death inducing ligand is from a distinctly different group of proteins, i.e. Bax, Bad, Bak and Bik and they differ amongst each other in that in Group VII the inducible vector system is introduced in a mixture of cells, while Group VIII is restricted to a group of cells that do express Fas and Group IX is restricted to a group of cells that do not express Fas.

Group X defines the special technical feature in that the cells into which the vector system is introduced are cells contained in a solid tumor. All the preceding groups were drawn to methods while the foregoing are drawn to compositions.

Group XI defines a special technical feature in that the expression vector comprises a tissue-specific inducible/conditional promoter, a feature not shared by previous groups. This feature is also anticipated by *Larregina et al.* Supra. Group XII defines a special technical feature in that the expression vector is tetracycline-responsive which is a feature not shared by any of the preceding groups.

Group XIII defines a special technical feature of the expression vector comprises a reporter protein (i.e. green fluorescent protein), a feature not shared by any of the previous groups. Group XIV defines a special technical feature where the expression vector comprises an encoded fusion protein causing tissue-specific localization of the target protein being expressed. This is distinct from a tissue-specific promoter where expression would occur in particular tissue, but the target would not necessarily be localized in the target tissue.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the

application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR .17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray Akhavan whose telephone number is 703-305-4454. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

DAVID GUZO
PRIMARY EXAMINER